Research letter

Minimal, superficial DNA damage in human skin from filtered far-ultraviolet C

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Dear Editor, Krypton chloride (KrCl) excimer lamps have a peak emission wavelength of 222 nm, in the ultraviolet (UV) C region of the electromagnetic spectrum. Currently KrCl lamps are the only viable 'far-UVC' sources for full-room inactivation of airborne SARS-CoV-2, the virus responsible for the COVID-19 pandemic.[1] Commercially available KrCl excimer lamps can be retrofitted to existing room lamp fittings or mounted at ceiling height independently. Other technologies, such as light-emitting diodes, are currently neither efficient nor powerful enough for such a task.

In addition to the peak KrCl excimer emission wavelength of 222 nm (83% at 200–230 nm), the lamp spectrum contains longer-wavelength UVC (10% at 230–280 nm), UVB (3%) and UVA radiation (4%). These additional wavelengths have been shown *in vivo* and *in silico* to penetrate to the skin's basal layer and cause DNA damage.[2,3] When the excimer lamp was filtered, reducing these longer wavelengths of UV radiation, a study in 20 healthy volunteers did not show erythema induction 24 h after exposure to 500 mJ cm^{-2}.[4] In that study there was a slight, statistically significant, increase in cyclobutane pyrimidine dimers (CPDs) compared with nonirradiated skin, although the location of these CPDs was not determined. However, computer modelling and animal experiments suggest that these CPDs will be limited in number and restricted to the uppermost parts of the epidermis.[2,5] The location of CPDs is important as, if limited to the superficial suprabasal nonproliferating skin cells, it is unlikely that this will indicate a carcinogenic risk.[6] To our knowledge, the location of CPDs from filtered far-UVC radiation, as described above, has never been demonstrated in human skin.

We performed human skin irradiation in two settings using a filtered KrCl far-UVC source (SafeZoneUVC, Ushio Inc., Tokyo, Japan): firstly, in a novel *ex vivo* full-thickness human skin model cultured at tension (manuscript in preparation) and secondly, using *in vivo* self-exposures. *Ex vivo* human skin was obtained from an abdominoplasty after full consent was obtained. This skin was cultured at the air–liquid interface in RM + medium containing 50 μg mL^{-1} gentamicin, 200 U mL^{-1} penicillin, 200 μg mL^{-1} streptomycin and 0·25 μg mL^{-1} amphotericin B. There were three samples: an unirradiated negative control sample, a positive control sample irradiated for 188 s delivering a radiant exposure of 515 mJ cm^{-2} narrowband UVB (peak emission wavelength 311 nm, TL01; Philips, Eindhoven, the Netherlands) and the test sample irradiated for 1000 s delivering a radiant exposure of 6100 mJ cm^{-2} filtered far-UVC. The human skin provider, Biopredic International, holds permit AC-2013-1754 granted by the French Ministry of Higher Education and Research for the acquisition, transformation, sales and export of human biological material for research.

In vivo, two of the authors irradiated their inner forearms at a dose of 6100 mJ cm^{-2} of filtered far-UVC, using the same irradiation source and distance as the *ex vivo* samples. Ethical approval was not required for self-exposures in the two senior investigators who led the *in vivo* aspects of this work.

Punch biopsies (4 mm) were taken from irradiated sites within 30 min of exposure and from nonirradiated sites, and were fixed in freshly prepared 4% paraformaldehyde at 20°C prior to paraffin embedding. CPD abundance was revealed by immunohistochemical staining with monoclonal anti-thymine dimer antibody (T1192; Sigma-Aldrich, St Louis, MO, USA).

Figure 1 displays histological staining of both the *ex vivo* and irradiated *in vivo* skin. As would be expected, there is CPD formation throughout the epidermis following narrowband UVB irradiation in the *ex vivo* skin model (Figure 1b) and no CPDs in the *ex vivo* control sample (Figure 1a). Both the *ex vivo* and *in vivo* filtered far-UVC-irradiated human skin samples show minimal CPD formation (Figure 1c and d, respectively). Where CPD-positive cells were present in one volunteer, importantly they were restricted to the upper layers of the epidermis, with no basal-layer CPD formation detected. Fewer CPD-positive cells were detected in the filtered far-UVC-irradiated skin of the second volunteer, where a thicker stratum corneum was evident, and both control *in vivo* samples were CPD negative (data not shown).

This first-in-human demonstration of CPD location from filtered far-UVC confirms the results of our previous *in silico* model and indicates that the peak KrCl excimer emission wavelength of 222 nm does not penetrate beyond the most superficial epidermal layers.[2] The *ex vivo* skin model was also in agreement with the *in vivo* exposures, enabling us to undertake future investigations that would be difficult to perform in humans. The radiant exposure delivered in these experiments is 265 times the current exposure limit value of 23 mJ cm^{-2} at 222 nm.[7] Therefore, even at very high exposure doses, appropriately filtered far-UVC is unlikely to present a carcinogenic risk through direct DNA damage. These important but preliminary results are very encouraging. As recently advised and encouraged by the UK's Scientific Advisory Group for

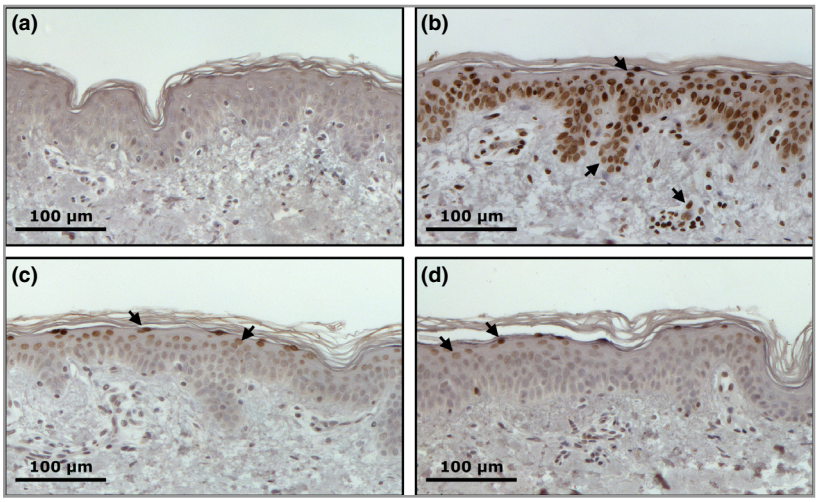

Figure 1 Histological staining. (a) Nonirradiated *ex vivo* skin sample. (b) Narrowband ultraviolet (UV)B-irradiated *ex vivo* skin sample. (c) Far-UVC-irradiated *ex vivo* skin sample. (d) Far-UVC-irradiated *in vivo* human skin sample. Formalin-fixed paraffin-embedded skin samples were stained for cyclobutane pyrimidine dimer (CPD) formation using immunohistochemical methods. Arrows are used to highlight examples of CPD-positive cells.

Emergencies we are continuing with multiple far-UVC research projects to investigate the efficacy and safety profile of this very promising technology.[8] However, to date, the evidence is overwhelmingly in favour of using filtered far-UVC as a safe, effective germicidal technology.

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